

**CALIFORNIA DEPARTMENT OF PESTICIDE REGULATION  
PUBLIC REPORT 2004-7**

**Famoxadone**

**Tracking ID 202589 N**

**DESCRIPTION OF ACTION**

E.I. Du Pont De Nemours & Company submitted an application seeking a California registration of DuPont Tanos Fungicide, EPA Reg. No. 352-604 to control certain plant diseases on potatoes, tomatoes, head lettuce cucurbits and peppers. DuPont Tanos Fungicide is a mixture of the new active ingredient, famoxadone and, an active ingredient found in currently registered pesticides, cymoxanil. DuPont Tanos Fungicide was registered by the U.S. Environmental Protection Agency (U.S. EPA) on August 27, 2003.

The Department of Pesticide Regulation (DPR) evaluated the product label and scientific data supporting registration of the product and found them to be acceptable to support conditional registration. The acute health risks from exposure to famoxadone are minimal due in part to its low mammalian toxicity. The precautionary and first aid statements on the product label, as well as label directions requiring personal protective equipment (PPE) and other protective measures adequately mitigate potential health risks to persons who may come in contact with the pesticide. DPR does not expect significant adverse environmental impacts to result from registration of this product.

**BACKGROUND**

Registrant:	E.I. DuPont De Nemours & Company
Common name:	Famoxadone
Chemical name:	5-methyl-5-(4-phenoxyphenyl)-3-(phenylamino)-2,4-oxazolidinedione
Brand name:	DuPont Tanos Fungicide
Uses:	To control diseases in potatoes, tomatoes, head lettuce, cucurbits and peppers.
Pests controlled:	Alternaria Leaf Blight, Anthracnose, Downy Mildew, Phytophthora blight, Early Blight, Late Blight, Septoria Leaf Spot, Gray Leaf Mold and Target Spot
Type of registration:	Conditional for fifteen year

DuPont Tanos Fungicide is formulated as a water dispersible granule with 25% famoxadone and 25% cymoxanil. As a combination of two fungicides with different modes of action, DuPont Tanos Fungicide can provide broad-spectrum control of several different plant diseases on a variety of crops. It can be used as a protectant because it inhibits spore germination. It can be also used as a curative because it inhibits mitochondrial respiration, specifically affecting the site of respiration the enzyme in fungus. DuPont Tanos Fungicide should be alternated with other fungicides, which have a different mode of action, following the resistance management program outlined on the label.

DuPont Tanos Fungicide can be applied to potatoes, tomatoes, head lettuce, cucurbits and peppers. Application rates range from 6-10 oz. per acre per application with seasonal maximums ranging from 36 oz. to 72 oz. depending on the crop with an annual maximum 72 oz. for all crops. The product can be applied as a broadcast treatment with ground, aerial or chemigation equipment. The minimum time interval between the last application and harvest is 14 days for potatoes and 3 days for the other crops. For crops not listed on the DuPont Tanos Fungicide label, there is a minimum 30-day waiting period after the last application before the other crops can be planted.

## SCIENTIFIC REVIEW

### **A. Chemistry**

1. Product Chemistry: DPR evaluated the submitted chemistry studies for the formulated product DuPont Tanos Fungicide and summarized the results in the following table.

**Table I. Physical and Chemical Properties of DuPont Tanos Fungicide**

Properties	Values
Physical state	Solid, granule
Density	0.58 g/mL 615 Kg/L g/cm <sup>3</sup>
Nominal concentration	25% Famoxadone 25% Cymoxanil
Certified limits	26.5, 23.5% Famoxadone 26.5, 23.5% Cymoxanil
Analytical technique	RP HPLC/UV
Vapor pressure (20°C)*	6.4x10 <sup>-7</sup> Pa (4.8 x 10 <sup>-9</sup> mmHg); 6.3 x 10 <sup>-12</sup> atm
Water solubility (pH=6.5 and 20°C)*	52, 143, 191, 243, 11, and 38 in unbuffered water.
Octanol/water partition coefficient (20°C)*	Log Kow = 4.6, 4.8, 4.6 and 5.6 at pH 3, 5, 7 and 9
Storage stability	Not submitted

\* These properties were derived using technical famoxadone as the test substance.

2. Residues in Food and Animal Feed: The submitted residue studies support the harvest and use limitations listed on the DuPont Tanos Fungicide label for potatoes, tomatoes, head lettuce cucurbits and peppers. The submitted data indicate the residues of famoxadone, cymoxanil and the metabolites are not likely to exceed the tolerance levels.

3. Environmental Fate: The famoxadone environmental fate studies which included: soil adsorption/desorption, hydrolysis, photolysis (aqueous and soil), aerobic and anaerobic soil metabolism, and terrestrial field dissipation were found to be satisfactory. Leaching and soil adsorption/desorption studies for famoxadone were conducted on three soil types. An additional soil type is required for unconditional registration. The submitted adsorption/desorption studies indicated slight mobility of famoxadone. The tendency of a pesticide to leach to groundwater

depends on its persistence in the environment, its solubility and how strongly it adsorbs to soil. Both U.S. EPA and DPR have developed sets of physicochemical criteria based on certain test types to estimate the potential of a chemical to leach to groundwater. The comparison indicates that famoxadone has a low potential for movement into groundwater.

The submitted product chemistry data, residue and environmental fate data support registration of DuPont Tanos Fungicide. The use of the product is expected to have minimal impact on the environment and it is not expected to leach into groundwater.

## B. Toxicology

E.I. Du Pont De Nemours & Company submitted adequate toxicology studies to conduct a complete toxicological evaluation of DuPont Tanos Fungicide. DPR evaluated the submitted data to ascertain the potential for adverse health effects from exposure to the pesticide. The acute toxicity parameters for DuPont Tanos Fungicide are summarized in Table II

**Table II. Acute Toxicity of DuPont Tanos Fungicide**

Type of Study	Acute Toxicity Values	Acute Toxicity Category
Acute oral	LD <sub>50</sub> =1311 mg/kg	III
Acute dermal	LD <sub>50</sub> >5000 mg/kg	IV
Acute inhalation	LC <sub>50</sub> >5.1 mg/l	IV
Primary eye irritation	N/A	IV
Primary dermal irritation	N/A	IV
Dermal sensitization	N/A	Not a dermal sensitizer
Signal word	N/A	CAUTION

\* N/A = Not Applicable

DPR's evaluation of the acute toxicity studies indicates that DuPont Tanos Fungicide is low in mammalian toxicity. The precautionary language on the product label adequately identifies the acute toxicity hazards noted in the studies.

DPR found the submitted toxicology studies sufficient to satisfy the data requirements of the Birth Defects Prevention Act (Food and Agricultural Code section 13121 et al). Possible adverse effects were observed in a dog and a monkey chronic toxicity study. Because neurotoxic symptoms were not observed during the acute and subchronic neurotoxicity studies, an acceptable developmental neurotoxicity study is not required at this time.

As a result of these findings, DPR has placed famoxadone in "low" priority for conducting a risk assessment. DPR prioritizes pesticide active ingredients for risk assessment based on the nature of the potential adverse health effects, number of potential adverse health effects, number of species affected, NOELs, potential for human exposure, use patterns, and similar factors. Based on these criteria, pesticides with the greatest potential for health problems are placed in high priority, with other chemicals being place in moderate or low priority. The purpose of the risk assessment will be to appraise the potential for famoxadone to cause adverse health effects in

humans if exposed to the pesticide as the result of a legal use. The potential for exposure from eating food crops treated with famoxadone will also be evaluated during the risk assessment. Further toxicity information is available in DPR's Summary of Toxicology Data for famoxadone, available on DPR public website at <http://www.cdpr.ca.gov/docs/toxsums/pdfs/5878.pdf>

### C. Health & Safety

An evaluation of the medical management information on the DuPont Tanos Fungicide label and the acute toxicity study results indicate the product label bears all of the required statements and warnings regarding safety to handlers and other persons who may be exposed to the pesticide. The product label bears an adequate first aid statement. In addition, the product label requires persons handling and applying DuPont Tanos Fungicide to wear long-sleeved shirt and long pants, chemical-resistant gloves category A (such as butyl rubber natural rubber, neoprene rubber or nitrile rubber) and shoes plus socks. Workers wearing only work clothing are not allowed to enter a treated field until 12 hours after an application for all crops. Persons entering a treated area before the 12 hour reentry interval has elapsed must wear coveralls, chemical-resistant gloves category A and shoes plus socks if they are going to contact treated plants, soil or water.

### D. Fish & Wildlife

The registrant submitted fish and wildlife toxicity studies, including studies on bobwhite quail, mallard duck, bluegill sunfish, rainbow trout, sheepshead minnow, *Daphnia magna* (water fleas), mysid shrimp, and oysters. The submitted data are adequate to characterize the toxicity to wildlife and aquatic animals from environmental exposure. Table III summarizes the results of these studies.

**Table III. Summary of Toxicity Studies for Wildlife**

Test Animal	Type of Study	Acute Toxicity Value**	Relative Toxicity
Bobwhite quail	Single acute oral dose	>2250 mg/kg (LD <sub>50</sub> )	Relatively non-toxic
Mallard duck	Feeding study (5 days)	>5620 ppm (LC <sub>50</sub> )	Relatively non-toxic
Bobwhite quail	Feeding study (5 days)	>5620 ppm (LC <sub>50</sub> )	Relatively non-toxic
Bluegill sunfish	Water exposure (96 hrs.)	>0.013 mg a.i./l (LC <sub>50</sub> )	Extremely toxic
Rainbow trout	Water exposure (96 hrs.)	0.011 mg a.i./l (LC <sub>50</sub> )	Extremely toxic
Sheepshead minnow	Water exposure (96 hrs.)	49.4 µg a.i./l (LC <sub>50</sub> )	Extremely toxic
<i>Daphnia magna</i>	Water exposure (48 hrs.)	12µg/l (EC <sub>50</sub> )	Extremely toxic
Mysid shrimp	Water exposure (28 days)	2.98 µg a.i./l (EC <sub>50</sub> )	Highly toxic
Oyster	Water exposure (96 hrs.)	1.41 µg a.i./l (EC <sub>50</sub> )	N/A
Honeybee	Acute contact (48 hrs.)	>25 µg/bee (LD <sub>50</sub> )	Slightly toxic

\* The test substance used for the studies was technical famoxadone.

\*\* Values expressed as : a. LD<sub>50</sub>= lethal dose that will kill 50% of test population; b. LC<sub>50</sub> =

lethal environmental concentration that will kill 50% of test population; and c.  $EC_{50}$  = Concentration that causes a specific effect in 50% of test population.

The data indicate famoxadone is relatively non-toxic to terrestrial wildlife, but highly toxic to freshwater fish and aquatic invertebrates. Label directions bear a warning indicating that the product is toxic to fish and aquatic organisms and prohibit application of the product directly to water, to areas where surface water is present or to intertidal areas below the mean high water mark.

Based on the submitted data, registered uses, label rates, and use restrictions for DuPont Tanos Fungicide, DPR does not expect toxic concentrations to occur in aquatic environments from use of the product in accordance with label directions.

### **E. Efficacy & Phytotoxicity**

Submitted data indicate that DuPont Tanos Fungicide provides control of various diseases on potatoes, tomatoes head lettuce, cucurbits and peppers. Applications of the product at rates higher than recommended on the product label did not result in significant phytotoxicity to crop plants. Phytotoxicity concerns regarding tank mixes are addressed on the product label, which advises that before using any tank mix, the user should test the combination on a small portion of the crop to be treated.

### **ALTERNATIVES**

U.S. EPA's PR Notice 2001-5 provides pesticide registrants with guidance regarding labeling for resistance management, and classifies different herbicides, fungicides, insecticides, etc. separately according to the mode or target site of action of the chemical. The classification of different chemicals by mode of action allows a user to alternate the usage of chemicals with different modes of action, thereby reducing the likelihood of developing resistance. Famoxadone is included in U.S. EPA's Fungicide/Bactericide Group #11. This group includes strobilurins and non-strobilurins. The biochemical mode of action of famoxadone is the inhibition of mitochondrial respiration. This mode of action is active against phenylamide (metalaxyl and oxadixyl) resistant Oomycete strains, an important consideration for the management of resistance to this class of fungicides. Unlike many of the competitive products, famoxadone and cymoxanil were not carcinogenic in rodent bioassays. Famoxadone will be a valuable resistance management tool for controlling several potentially devastating diseases, such as late blight, early blight and downy mildew, while maintaining current disease management systems.

Repeated use of the same fungicide or fungicides with similar modes of action can result in the failure to control plant pathogenic fungi, allowing them to reproduce and generate resistant fungi populations. The registration of famoxadone provides an alternative fungicide that can be used in resistance management programs with other fungicides that have other alternative modes of action.

### **CONCLUSION**

DPR evaluated the product label and scientific data submitted to support the registration of DuPont Tanos Fungicide and found them acceptable to support conditional registration. The precautionary and first aid statements on the product label, as well as the required PPE and other protective measures mitigate potential health risks to persons who may be exposed to the pesticide. If, after the risk assessment, DPR determines that exposure to famoxadone may result in unacceptable margins of exposure, further restrictions will be placed on the use of famoxadone at that time. Submitted data also indicate that no significant adverse environmental impacts are expected to occur from the use of DuPont Tanos Fungicide and that when used in accordance with label directions, the product will be effective for its intended use.

DPR is proposing a 15-month conditional registration of DuPont Tanos Fungicide. The registrant is required to conduct and submit the results of the following studies: (1) a one-year storage stability study; and (2) a soil adsorption/desorption study on an additional soil type (silt loam).